103* How long can aminoglycosides be deferred using β-lactam alone for *Pseudomonas aeruginosa* (PA) in children with CF?

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Aims: To study the time to emergence of ceftazidime (Caz) resistant *P. aeruginosa* (r-PA) in patients managed through childhood with elective intravenous antibiotic regimen and preference for monotherapy with this antibiotic.
Methods: Children diagnosed with CF since 1982 and found to have PA were studied retrospectively (27 m, 28 f). Patients were managed at a tertiary centre with elective 3-monthly IV antibiotic regimen for 1st isolation of PA (1st PA) until PA clearance (no PA in the preceding 12 m) and again for PA colonization. For each course, treatment was determined from the PA susceptibility pattern over the preceding 3 m, the preference being Caz. Aminoglycosides were added to the treatment regimen when Caz r-PA emerged. Sputum results were examined for 1st PA; PA clearance, PA colonization (repeated and persistent isolation); and Caz r-PA.
Results: Results are shown in the table.

	n	median (range), y
Age at 1st PA	55	2.1 (0.3–7.9)
Age at PA colonisation	43	6.7 (0.5–14.8)
Age at Caz resistant PA	37	10.1 (2.5–15.5)
Interval to Caz resistant PA after colonisation	35	2.6 (0.1–11.8)

At 1st PA, none were resistant to Caz. 18/55 patients had no PA clearance and thus had colonization from 1st PA. 37/55 had PA clearance after treatment for 1.3 y (1–5) and of these, 25 had PA colonization after a PA free period of 6.5 y (1.2–14.5). Two patients had Caz r– PA at start of colonization.
Conclusions: In comparison to alternative regimens including aminoglycosides from colonization, a regimen with a preference for monotherapy with Caz permitted deferring the addition of aminoglycosides by a median duration of 2.6 years. Thus patients were spared aminoglycosides and the cumulative dose was reduced by an average of 10 courses.

104 A longitudinal study of the antimicrobial resistance of *Pseudomonas aeruginosa* in a Turkish CF Unit

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Introduction: An important consequence of antibiotic therapy of chronic *Pseudomonas aeruginosa* (PA) infection in CF is the increasing rate of antibiotic resistance. This study was aimed to investigate the rate of antibiotic resistance in PA isolated from a group of Turkish CF patients.
Methods: A total of 195 CF patients were retrospectively analysed for PA isolation rate and susceptibility. The in vitro efficacy of aztreonam, ceftazidime, cefepime, imipenem, amikacin, tobramycin and ciprofloxacin against PA isolated between 1995–2005 were investigated by disk diffusion susceptibility testing according to CLSI guidelines. Data were analyzed in terms of resistance on 5 yearly basis. One to three isolates with different phenotypic characteristics/year/patient were considered for the analysis.
Results: PA was isolated from 93 cases (47.7%). The number of isolates were 35 in 1995, 49 in 2000 and 113 in 2005. The rates of resistances were given in the table. Multiresistant isolates were 5.7% in 1995, 4% in 2000 and 8.9% in 2005. Inducible beta-lactamase activity was detected in 20.4% of isolates in 2000 and 30.0% in 2005.

Antibiotics	1995 (% R)	2000 (%R)	2005 (%R)
Aztreonam	17.1	26.5	29.2
Ceftazidime	20.0	14.3	27.4
Cefepime	–	12.2	15.0
Imipenem	5.7	12.2	16.8
Amikacin	11.4	18.4	11.5
Tobramycin	–	22.4	14.1
Ciprofloxacin	8.6	12.2	13.3

Conclusion: This study indicates the increasing resistance especially to beta-lactam antibiotics amongst PA isolates in our CF population. The decreasing rate of resistance to aminoglycosides may be attributed to the use of inhaled tobramycin starting from the end of 2004. The prudent use of antibiotics and monitorization of resistance should be actively considered.

105* The determination of the synergistic antibiotic combinations for the treatment of multiresistant *Pseudomonas aeruginosa* isolates from CF patients

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Introduction: Treatment failure due to antibiotic resistant *Pseudomonas aeruginosa* (PA) is a frequent outcome in CF. The best therapeutic approach for the treatment of such infections seems to be the use of combination antibiotic therapy. The aim of this study is to determine the optimal bactericidal combination by multiple combination bactericidal testing (MCBT) for multiresistant CF PA isolates.
Methods: The bactericidal activities of 40 multiresistant PA isolates were determined for single and double antibiotics, to give 19 different combinations, by MCBT using fixed antibiotic concentrations based on estimates of the average peak levels in serum after single iv administration. Tobramycin 200 μg/ml denoted the concentration in lungs after inhalation.
Results: The % bactericidal activity of single antibiotics against the test isolates were: aztreonam 27.5, ceftazidime 27.5, cefepime 40, meropenem 75, ciprofloxacin 77.5, amikacin 75, tobramycin 4 μg/ml 77.5, tobramycin 200 μg/ml 92.5. Combination testing revealed that ciprofloxacin+tobramycin 200 and meropenem+amikacin were 95% bactericidal, followed by cefepime+amikacin 92.5%, meropenem+tobramycin 200 (87.5%), cefepime+tobramycin 200 85%, ciprofloxacin+amikacin 77.5%, ciprofloxacin+ceftazidime 72.5%.
Conclusion: Double antibiotic combinations are more likely than single antibiotics to be bactericidal in vitro against multiresistant PA. The most effective combinations in our CF PA population were ciprofloxacin+inhaled tobramycin (200 μg/ml) and meropenem+amikacin. Overall data indicated that inhaled tobramycin significantly enhanced the bactericidal activity of the second drug.

106 Mucoid phenotype of *Pseudomonas aeruginosa* isolates is associated with decreased antimicrobial resistance

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Introduction: The majority of adult patients with cystic fibrosis (CF) are colonized with *Pseudomonas aeruginosa* and a significant proportion of them have a mucoid phenotype. Some studies have shown the mucoid phenotype to be associated with increased antimicrobial resistance [1] whereas others have found decreased antimicrobial resistance [2].
Aims: We audited retrospective resistance data from our CF population to investigate the association between mucoid phenotype and antimicrobial resistance.
Methods: Data from 1876 *P. aeruginosa* isolates, from 194 adult CF patients, were analyzed and the percentage of antibiotics (usually a standard panel of 9) to which they had been tested and found resistant, according to standard disc-diffusion method on agar, was recorded.
Results: There were 1061 mucoid isolates and 815 non-mucoid isolates. The median percentage of antibiotics to which the isolates were resistant was 0% (inter-quartile range 0–22%) for the mucoid isolates and 44% (interquartile range 0–100%) for the non-mucoid isolates ($p < 0.001$). For each of the 9 antibiotics, non-mucoid isolates were significantly more likely than mucoid isolates to be resistant ($p < 0.001$).
Conclusions: Non-mucoid isolates were significantly more resistant to antimicrobials than mucoid isolates. This may be because mucoid isolates are protected from antimicrobials in vivo by the mucoid alginate and therefore lose the more typical antibiotic resistance systems needed to confer resistance when tested in-vitro.

References

[1] Govan, J.R. and J.A. Fyfe, J Antimicrob Chemother 1978; 4: 233–40.
[2] Demko, C.A. and M.J. Thomassen, Curr. Microbiol. 1980; 4: 69–73.